FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 06:21:17 ON 01 OCT 2007

L1 647 S (N-ACETYLGLUCOSAMINYLTRANSFERASE III) OR (GNT III) OR (GNT-II
L2 33 S L1 (P) (FUSION OR CHIMERA OR CHIMERIC)
L3 13 DUP REM L2 (20 DUPLICATES REMOVED)
L4 53 S L1 AND (FUSION OR CHIMERA OR CHIMERIC)
L5 36 S L4 AND (IGG OR ANTIBOD? OR IMMUNOGLOBULIN)
L6 12 S L5 AND ((MANNOSIDASE II) OR (MANN II))
L7 5 S L3 AND ((MANNOSIDASE II) OR (MANN II))
L8 9 DUP REM L6 (3 DUPLICATES REMOVED)

IN Umana, Pablo; Jean-Mairet, Joel; Bailey, James E.
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
TI Glycosylation engineering of antibodies for improving antibody-dependent cellular cytotoxicity
AB The present invention relates to the field of glycosylation engineering of proteins. More particularly, the present invention is directed to the glycosylation engineering of proteins to provide proteins with improved therapeutic properties, e.g., antibodies, antibody fragments, or a fusion protein that includes a region equiv. to the Fc region of an Ig, with enhanced Fc-mediated cellular cytotoxicity. The antibodies or fusion proteins with enhanced Fc-mediated cellular cytotoxicity are expressed in host cells engineered to also express a glycoprotein-modifying glycosyl transferase, e.g. .beta.(1,4)-N-acetylglucosaminyltransferase III or V, .beta.(1,4)-N-galactosyltransferase, and mannosidase II .

IN Umana, Pablo; Bruenker, Peter; Ferrara, Claudia; Suter, Tobias
SO PCT Int. Appl., 231 pp.
CODEN: PIXXD2
TI Engineering of glycosylation profile of antibody Fc region to increase Fc receptor binding affinity and effector function for treating cancer
AB The present invention relates to nucleic acid mols., including fusion constructs, having catalytic activity and the use of same in glycosylation engineering of host cells to generate polypeptides with improved therapeutic properties, including antibodies with increased Fc receptor binding and increased effector function. The engineered proteins or antibodies comprise Golgi localization domain of Golgi resident polypeptide such as .beta.(1,4)-N-acetylglucosaminyltransferase III, .beta.(1,4)-galactosyltransferase, mannosidase II, .beta.(1,2)-N-acetylglucosaminyltransferase I, .beta.(1,2)-N-acetylglucosaminyltransferase II, mannosidase I, .alpha.-mannosidase II, and .alpha.1-6 core fucosyltransferase. The effector function includes Fc-mediated cellular cytotoxicity of NK cells, macrophage, polymorphonuclear cells and monocytes; signaling of apoptosis induction; maturation of dendritic cells; or T cell priming. The engineered antibodies include antibodies or humanized antibodies specific to human neuroblastoma, renal cell carcinoma, colon carcinoma, breast carcinoma, lung carcinoma, 17-1A antigen, CD20, CD22, CD30, CD40, PSMA, EGFR, PSCA, HLA-DR, MUC1, EpCAM, etc.

AU Ferrara Claudia; Brunker Peter; Suter Tobias; Moser Samuel; Puntener Ursula; Umana Pablo
SO Biotechnology and bioengineering, (2006 Apr 5) Vol. 93, No. 5, pp. 851-61.
Journal code: 7502021. ISSN: 0006-3592.
TI Modulation of therapeutic antibody effector functions by glycosylation engineering: influence of Golgi enzyme localization domain and co-expression of heterologous beta1, 4-N-acetylglucosaminyltransferase III and Golgi alpha-mannosidase II.
AB The effector functions elicited by IgG antibodies strongly depend on the

carbohydrate moiety linked to the Fc region of the protein. Therefore several approaches have been developed to rationally manipulate these glycans and improve the biological functions of the antibody. Overexpression of recombinant beta1,4-N-acetylglucosaminyltransferase III (GnT-III) in production cell lines leads to antibodies enriched in bisected oligosaccharides. Moreover, GnT-III overexpression leads to increases in non-fucosylated and hybrid oligosaccharides. Such antibody glycovariants have increased antibody-dependent cellular cytotoxicity (ADCC). To explore a further variable besides overexpression of GnT-III, we exchanged the localization domain of GnT-III with that of other Golgi-resident enzymes. Our results indicate that chimeric GnT-III can compete even more efficiently against the endogenous core alpha1,6-fucosyltransferase (alpha1,6-FucT) and Golgi alpha-mannosidase II (ManII) leading to higher proportions of bisected non-fucosylated hybrid glycans ("Glyco-1" antibody). The co-expression of GnT-III and ManII led to a similar degree of non-fucosylation as that obtained for Glyco-1, but the majority of the oligosaccharides linked to this antibody ("Glyco-2") are of the complex type. These glycovariants feature strongly increased ADCC activity compared to the unmodified antibody, while Glyco-1 (hybrid-rich) features reduced complement-dependent cytotoxicity (CDC) compared to Glyco-2 or unmodified antibody. We show that apart from GnT-III overexpression, engineering of GnT-III localization is a versatile tool to modulate the biological activities of antibodies relevant for their therapeutic application. (c) 2006 Wiley Periodicals, Inc.

IN Bobrowicz, Piotr; Hamilton, Stephen R.; Gerngross, Tillman U.; Wildt, Stefan; Choi, Byung-Kwon; Nett, Juergen Hermann; Davidson, Robert C.

SO PCT Int. Appl., 193 pp.
CODEN: PIXXD2

TI N-acetylglucosaminyltransferase III and other N-glycan-processing enzymes expressed in lower eukaryotes for the biosynthesis of human-like oligosaccharide structures in glycoproteins

AB The present invention relates to eukaryotic host cells having modified oligosaccharides which may be modified further by heterologous expression of a set of glycosyltransferases, sugar transporters, and mannosidases to become host-strains for the prodn. of mammalian, e.g., human therapeutic glycoproteins. The process provides an engineered host cell such as Pichia pastoris which can be used to express and target any desirable gene(s) involved in glycosylation. Host cells with modified lipid-linked oligosaccharides are created or selected. N-glycans made in the engineered host cells exhibit N-acetylglucosaminyltransfera se III (GnTIII) activity, which produce bisected N-glycan structures and may be modified further by heterologous expression of one or more enzymes, e.g., glycosyltransferases, sugar transporters and mannosidases, to yield human-like glycoproteins. For the prodn. of therapeutic proteins, this method may be adapted to engineer cell lines in which any desired glycosylation structure may be obtained.

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("5874271").PN.	USPAT	OR	OFF	2007/10/01 04:14
L2	2	neorx451	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 04:14
L3	0	WO adj "199810062"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 04:15
L4	3	WO adj "9810062"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 04:16
L6	226	(N-acetylglucosaminyltransferase adj III) OR (Gnt adj III) OR (Gnt-iii) OR Gnt3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 05:54
L7	24	l6 same (fusion or chimera)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 05:55
L8	24	l7 and (antibod? or immunoglobulin OR igg)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 05:55
L9	157	l6 and (fusion or chimera or chimeric)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 05:56
L10	153	l9 and (antibod? or immunoglobulin OR igg)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 05:55
L11	148	l10 and ((mannosidase adj II) OR (mann II))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 05:56
L12	25	l6 same (fusion or chimera or chimeric)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 06:00
L13	26240	((mannosidase adj II) OR (mann II)) same (fusion or chimera or chimeric)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 05:57
L14	104	l11 and (ADCC OR fc adj mediated)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/10/01 05:58

EAST Search History

S1	22	Pablo near2 umana.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/28 11:16
S2	5	peter near2 bruenker.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/25 11:30
S3	1	WO adj "200131045"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/25 11:31
S4	1	WO adj "200129242"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/28 15:29
S5	0	WO adj "199954342"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/25 11:32
S6	5	WO adj "9954342"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/25 11:32
S7	8	claudia near2 ferrara.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/25 11:46
S8	6	tobias near2 suter.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/28 11:17
S9	4	ronald near2 bassuner.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/28 16:16
S10	1	siva near2 manjunath.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/28 16:18
S11	5	douglass near2 russell.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/09/28 16:18